

# Regulatory Writing

SECTION EDITOR



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## Authorship issues in regulatory documents



When medical writers discuss authors and authorship – the theme of this issue of medical writing – they are usually referring to documents in the public domain such as journal articles or maybe congress abstracts. The primary purpose of such publications is to communicate the results of the study to the scientific community and wider world. The investigators who appear as authors of an article about a clinical trial should rightly take responsibility for the content. Thus, all authors should have been

involved in the drafting process, and have critically reviewed and approved a manuscript prior to publishing. They may have requested additional outputs to be generated or suggested that certain conclusions are toned down or changed. They should also have had access to the data to verify the presentation of the results and the conclusions. But large volumes of outputs are generated and in the real world where investigators are busy clinicians, only the most diligent will have gone through

the source data in detail. Potential conflicts of interest should be declared and the involvement of a medical writer should be acknowledged. Given that drug development takes place in a competitive environment and that the temptation to present results in a favourable light is strong, the aim of the above is to prevent ghost-written articles. In the past, such articles have used the veneer of peer-reviewed respectability for marketing ends. Greater awareness of these issues,

combined with stringent public disclosure requirements, giving readers access to the results pertaining to the main efficacy endpoints and safety, have no doubt reduced the extent of these dubious practices, though there is always room for improvement.

### Realities of clinical research

Although the investigators named as authors take public responsibility for the article content, there is a tacit recognition (perhaps not always addressed in discussions about journal authorship) that the study design and analysis is largely done by the drug company. So although the investigators will have been the ones who actually administered the study drug to the patients, in terms of the big picture, a team within the company, involving many employees with expertise in many different areas (biostatistics, clinical science, clinical pharmacology, and so on) will have been responsible for study design and administrative aspects. The company will have drafted the protocol (although investigators may have provided input to study design through participation in steering committees and advisory boards). Likewise, the statistical outputs will be produced within the company, and drafting the clinical study report (and public disclosure of the results on a clinical trial registry if appropriate) will also be the responsibility of the company.

### Authorship of regulatory documents

Unlike journal articles, regulatory documents are generally prepared for submission to the health authorities and are not available in the public domain (although this may be changing with the current shift towards greater transparency). Companies will have well defined Standard Operating Procedures that describe exactly who is responsible for reviewing and/or approving a document or sections of a document. The medical writer assigned to the project is not an intellectual author in the sense that authors of journal articles are (or should be), but rather has a more technical role. The responsibility of the medical writer is mainly to compile and present data from a wide range of sources and ensure that regulatory documentation requirements are met. As a result, there is usually no need to name a medical writer as an author, or explicitly acknowledge his or her participation in the document, which if the appropriate review and approval cycles

have been followed should reflect a consensual company position.

The target audience, the health authority reviewers, is aware of the conflict of interest (the company will ultimately want to see the drug approved) and so the documents will generally be read with a critical eye. Audits can ensure the accuracy of the data and health authorities have the option of asking further questions in many types of interactions. If it transpires that the company has attempted to mislead the health authorities, the consequences both financially and in terms of loss of faith and credibility can be severe. From my experience, companies take their interactions with the health authorities very seriously and “we can’t be seen to be hiding anything” is a common sentiment in discussions about data presentation to the health authorities. Certainly (and again I am speaking about my personal impression), companies nowadays show plenty of apprehensive respect to the regulators who can make life very difficult for a company.

### Investigator conformity in regulatory documents

Although most regulatory documents are authored and approved internally, a company must sometimes seek the signature or approval of someone external to the company. For example, as per International Conference on Harmonisation (ICH) guidance, clinical study reports (CSRs) must be accompanied by the signature of the principle investigator (for a single-centre trial) or the coordinating investigator (in the case of multicentre trials). The regulations are rather vague as to who should be designated the coordinating investigator. For example, ICH E3 states that the figure of the coordinating investigator will usually be designated by the protocol. However, the wording does not make this obligatory and, in practice, the protocol is often silent on this matter. If the study has a Data Safety Monitoring Board (DSMB) or some other study oversight body, then one common practice is for the DSMB chair to be made coordinating investigator. Another approach might be to ask the investigator who has recruited most patients. Either way, the final decision often has a political dimension. For example, if a publication is planned from the results of the study, then the lead author and the coordinating investigator may be one and the same.

The investigator signature page essent-

ially confirms that to the best of his or her knowledge, the trial was conducted according to Good Clinical Practice and that the results presented reflect those obtained. Unlike the author of a publication, the investigator doesn’t necessarily have to fully agree with the interpretation of the results to sign the investigator signature page, just acknowledge that the study was appropriately conducted and that the results themselves are accurate. In any case, detailed interpretation of the results is not usually included in the discussion section of a CSR. Although decisions about which results are highlighted and how they are presented in the text of the CSR may influence the readers’ perception of the study, the most important outputs are appended to the document and will be available to reviewers. Thus, CSRs are essentially factual documents with limited opportunity for spin.

Higher level documents do of course include company interpretation of the data. The clinical overview, for example, may aim to convince the regulators that the company’s product should be approved. The regulators, for their part, have extensive access to supporting data and can make up their own minds. Indeed, the Food and Drug Administration takes a bottom-up approach, paying relatively little attention to the higher level documents anyway and performing their own analyses of the raw data.

### Journal articles and regulatory documents – two different worlds

In short, clinical development is a complex, collaborative process involving many company employees, hired external workers, and of course the investigators and other medical staff. Journal articles describing an interventional trial generally aim to disseminate the results. The limited number of authors who take public responsibility for the article content may not accurately reflect the extent of the effort or the real intellectual input. Regulatory documents, in contrast, if authored and reviewed according to company guidelines, with input from the relevant departments, should provide an accurate and detailed description of the clinical development process and represent the company position. The role of the regulatory medical writer is a technical one, and there is usually no need to acknowledge his or her input.

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